

## Consensus statement

**Supplementary file Module 2****Scoping question**

How is Achilles tendinopathy diagnosed?

**Literature search and selection***Sub-question 1 (diagnostic criteria)*

In order to answer sub-question 1, a systematic literature search was carried out using the following question:

What are the criteria for diagnosing Achilles tendinopathy?

The systematic literature analysis was performed using the following PICO:

- P:** patients with a suspected Achilles tendinopathy;
- I:** diagnostic criteria in patients with Achilles tendinopathy;
- C:** diagnostic criteria in patients without Achilles tendinopathy;
- O:** test properties (sensitivity, specificity and predictive value) of the diagnostic criteria.

The working group considered the diagnostic criteria for Achilles tendinopathy to be the primary outcome measure for sub-question 1. The working group considered imaging findings not to be suitable outcome measures, as abnormalities on imaging can also occur in asymptomatic individuals. Imaging is described separately in Module 3.

On January 10<sup>th</sup> 2019, a PICO based systematic literature search (Table 2.1) was carried out in collaboration with the Medical Librarian of Erasmus MC within the following databases: Embase, Medline Ovid and Cochrane CENTRAL. Relevant studies were selected based on the following criteria.

**Inclusion criteria:**

- The study evaluated properties (sensitivity, specificity and predictive value) of clinical tests for diagnosing Achilles tendinopathy.
- The study had a cohort or cross-sectional research design.

**Exclusion criteria:**

- The study was an animal study or has an in vitro research design.
- The study included  $\leq 10$  patients.

In addition, national and international guidelines were reviewed: the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007), the guideline databases of the Dutch General Practitioners Society (NHG), the National Institute for Health and Care Excellence (NICE), the National Guidelines Clearinghouse (NGC) and the Guidelines International Network (G-I-N).

In addition to the database search, the diagnostic criteria used in the included randomised trials in the treatment module were reviewed. For more information about the search, the working group refers to the Treatment module (Module 4).

**Results**

A flow chart of the selection process is displayed in Figure 2.1. The results of the database search consisted of 343 articles of which 69 were considered potentially relevant based on title and abstract screening. In addition, in three (systematic) reviews and guidelines the reference list was screened for relevant studies<sup>1-3</sup>, after which 1 additional potentially relevant article was added. After examining the full text of these 70 articles, none of the studies were found to meet the pre-established criteria. Therefore, the GRADE methodology was not used. A review of the existing national and international guidelines revealed no useful results.

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Information from existing guidelines will also be taken into account. The diagnostic process for diagnosing Achilles tendinopathy has been discussed in 2 guidelines: previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007) and the American Physical Therapy Association.<sup>4</sup>

31 studies were included in the Treatment module (Module 4). The majority focused on patients with midportion Achilles tendinopathy (26 studies). The other studies focused on patients with insertional Achilles tendinopathy (3 studies) and patients with Achilles tendinopathy where the location was not specified (2 studies).

#### *Midportion Achilles tendinopathy*

The criteria used in 26 studies to clinically diagnose midportion Achilles tendinopathy are shown in summary in Table 2.2 and in detail in Table 2.4. The 3 most used criteria were pain on palpation (17/26 studies), symptoms localised 2 to 7 cm proximal from the Achilles tendon insertion (13/26 studies) and thickening of the Achilles tendon (11/26 studies).

In 14 out of these 26 studies (54%) imaging modalities (ultrasound or MRI) were used in the diagnostic process.

#### *Insertional Achilles tendinopathy*

The criteria used in 3 studies to clinically diagnose insertional Achilles tendinopathy are shown in summary in Table 2.3 and in detail in Table 2.4. In 2 studies, pain on palpation of the Achilles tendon insertion and a reduced tendon loading capacity were used as criteria. In 1 study no diagnostic criteria were reported.

In two out of three studies (67%) in patients with insertional Achilles tendinopathy, ultrasound was used in the diagnostic process.

#### Quality of evidence

As these criteria were not outcome measures in studies but more a reflection of the expert opinion in diagnosing Achilles tendinopathy, the quality of the evidence was not assessed using the GRADE system.

#### Sub-question 2 (Differential diagnoses)

For answering sub-question 2, we designed the following question:

Which differential diagnoses of posterior ankle pain should be considered and which underlying pathology might be related to Achilles tendinopathy?

#### Methods

The working group decided not to use a systematic literature review to answer sub-question 2, but to review existing guidelines, (inter)national guideline databases, sports medical books, systematic reviews and the expertise of the working group. Therefore, the previous Dutch multidisciplinary chronic Achilles tendinopathy guideline (2007), the guideline of the Orthopaedic Section of the APTA<sup>4</sup> and the 'Clinical Sports Medicine' book (5<sup>th</sup> edition, 2017) were consulted. No systematic reviews were found that describe the differential diagnosis of Achilles tendinopathy.

#### Results

Table 2.5 displays the differential diagnoses that can be considered in posterior ankle pain, suggestive for Achilles tendinopathy.

Table 2.6 displays the potentially associated pathologies for Achilles tendinopathy, based on the criteria identified in sub-question 1.

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**Conclusions**

*Sub-question 1. What are the criteria for diagnosing Achilles tendinopathy?*

## Midportion and insertional Achilles tendinopathy

<b>- Grade</b>	There are no data available on the test characteristics of diagnostic criteria.
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## Midportion Achilles tendinopathy

<b>- Grade</b>	<p>The most commonly used criteria for diagnosing midportion Achilles tendinopathy in randomised trials are:</p> <ol style="list-style-type: none"> <li>1) Pain on palpation</li> <li>2) Symptoms localised 2 to 7 cm proximal to the tendon insertion</li> <li>3) Thickening of the tendon</li> <li>4) Pain during or after exercise</li> </ol> <p>In 54% of RCTs, imaging (ultrasound or MRI) was used as part of the diagnostic process.</p>
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## Insertional Achilles tendinopathy

<b>- Grade</b>	<p>The most commonly used criteria for diagnosing insertional Achilles tendinopathy in randomised trials are:</p> <ol style="list-style-type: none"> <li>1) Pain on local palpation.</li> <li>2) Reduced loadbearing capacity of the tendon.</li> </ol> <p>In 67% of RCTs, imaging (ultrasound) was used as part of the diagnostic process.</p>
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*Sub-question 2. Which differential diagnoses of posterior ankle pain should be considered and which underlying pathology might be related to Achilles tendinopathy?*

## Midportion and insertional Achilles tendinopathy

<b>- Grade</b>	Based on the expertise of the working group, existing guidelines and (sports) medical literature, differential diagnostic considerations for posterior ankle pain (Table 2.5) and for possibly associated pathologies in midportion and insertional Achilles tendinopathy (Table 2.6) are summarised.
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**Considerations**

The working group concludes that a number of clinical diagnostic criteria can be used for both insertional and midportion Achilles tendinopathy. There is disagreement in general and within the working group about the use of imaging in the diagnostic process. A broad differential diagnosis has been formulated for both patients with posterior ankle complaints suggestive of Achilles tendinopathy, as well as possibly related underlying pathology in patients with clinically diagnosed Achilles tendinopathy.

An extensive search in literature revealed no available data on the sensitivity, specificity and predictive values of specific diagnostic tests to diagnose Achilles tendinopathy. This is a limitation in formulating recommendations for the diagnosis of Achilles tendinopathy. Although, it is also questionable what should be considered as 'gold standard' for diagnosing Achilles tendinopathy.<sup>5</sup> Previous guidelines and a recently published international consensus statement shows a consensus for using a clinical diagnosis. Among 28 international experts in tendinopathy and 32 patients with tendinopathy there was consensus that Achilles tendinopathy should be defined by the following characteristics: 'pain and loss of function related to loading'.<sup>6</sup> The working group acknowledges that this consensus meeting focused mainly on terminology of the condition and not on the specific associated diagnostic criteria. The ICON consensus group also

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stated that clinical findings should be assessed appropriately (e.g. when pain on palpation is assessed, the exact location of the pain and the palpated structure should be clearly defined).<sup>7</sup> The survey of the Netherlands Patient Federation on the diagnostic process found that the majority of the 96 respondents (92%) were diagnosed clinically. This may well be due to the fact that imaging abnormalities can be present in the asymptomatic population.<sup>1</sup> As a result, a simple imaging gold standard is not available. On the other hand, the absence of abnormalities on imaging may preclude the diagnosis of Achilles tendinopathy. Although imaging abnormalities in an early reactive tendinopathy may still be lacking, chronic tendinopathy can be characterised by tendon thickening and structural abnormalities on imaging. In the absence of these findings on imaging, the working group recommends reconsidering the diagnosis. Due to the above-mentioned data, the role of conducting diagnostic imaging for Achilles tendinopathy is complex. Imaging is covered in more detail in Module 3.

Due to the lack of evidence for the use of a (number of) specific tests to diagnose Achilles tendinopathy, the working group has chosen to extract the diagnostic criteria from inclusion criteria used in RCTs on Achilles tendinopathy. This recognises the opinions of expert clinicians and researchers in diagnosing Achilles tendinopathy. The group felt that this justified the use of conclusions of these trials in formulating recommendations in the guideline. Most studies described the diagnostic criteria for midportion Achilles tendinopathy (n=26) and a few for insertional Achilles tendinopathy (n=3). A number of diagnostic criteria were used more frequently than others, and the working group used a cut off value of more than 30% for criteria to be incorporated in the recommendations.

History taking and physical examination are important elements to diagnose Achilles tendinopathy. There should be localised pain, which increases with more tendon-loading activities. The localisation of pain in the Achilles tendon can be acquired reliably on history taking between clinicians.<sup>8</sup> Tendon thickening, on physical examination, is another frequently used diagnostic criterion and has good to moderate reliability.<sup>8</sup> It is debatable whether pain on palpation should be used as diagnostic criterion. Pain on patellar tendon palpation was present in 46% of asymptomatic jumping athletes.<sup>9</sup> While this should make the examiner alert to potential false-positive findings, the clinical situation is different when a patient has a history of localised pain and the pain on local palpation is recognisable. Assessment of pain on palpation can be performed with very good intra-rater and good inter-rater reliability.<sup>8</sup> These data show that these simple clinical diagnostic criteria are reliable to assess.

The working group discussed that local thickening should also be added to the diagnostic criteria for insertional Achilles tendinopathy as well as a reduced loadbearing capacity of the tendon, which is considered to result of pain on activity. The working group believes that for insertional tendinopathy the relationship between (sports) loading and symptoms should be part of these diagnostic criteria.

The working group considers it important to mention that these clinical diagnostic criteria might be less applicable for Achilles tendinopathy with short symptom duration, as almost all the included randomised studies have included patients with chronic symptoms. A proportion of patients with short-lived symptoms might have similar clinical diagnostic criteria as those with chronic Achilles tendinopathy. Some patients might – however – have a different clinical picture (e.g. absence of tendon thickening). It is questionable whether these patients should be labelled as having Achilles tendinopathy.<sup>5</sup>

Considering patients with possible Achilles tendinopathy who present with posterior ankle pain, the working group found it important for healthcare providers to consider a broad differential diagnosis. It is outside the scope of this guideline to formulate a more extensive detailed list of potential diagnoses. Table 2.5 presents the differential diagnoses that the working group recommends considering when assessing these patients. It is important to note that the clinical importance of an associated bursitis, Haglund's morphology, intratendinous calcifications, plantaris tendon-mediated Achilles tendinopathy and peritendinous abnormalities of the Achilles

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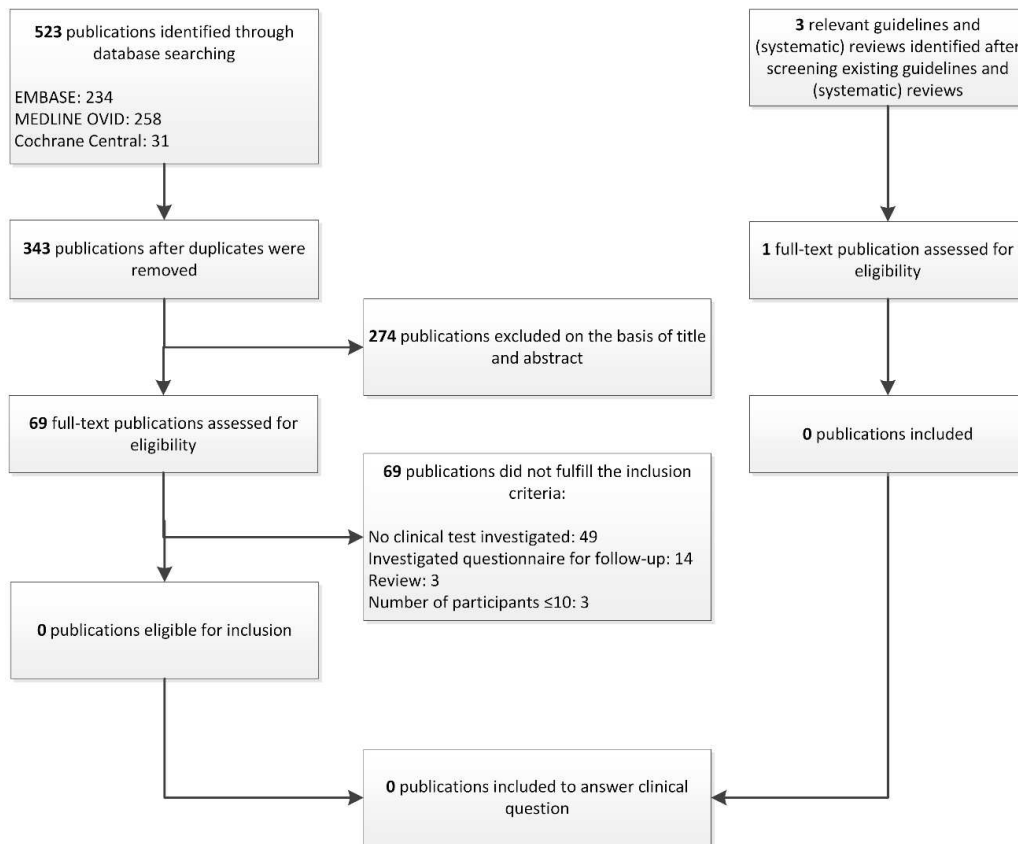
tendon is not clearly established. The working group recognised that possible associations could be present between these findings and Achilles tendinopathy. These might also be a specific target for treatment. It is unknown whether these conditions have a different prognosis or if patients benefit from specific targeted treatments in these cases. Due to the presumed relationship between these abnormalities on imaging and the Achilles tendon, a causal relationship might be considered, but it is often complex to establish this as many of these imaging findings also occur in asymptomatic individuals.

Once a diagnosis of Achilles tendinopathy is established, the working group advises considering underlying pathologies or diseases which may have specific consequences on general health or in which specific treatments are available. Enthesitis related to auto-inflammatory arthropathies and tendon xanthomas as part of Familial Hypercholesterolemia are clear examples and further explained in Table 2.7. The working group recommends referring to appropriate medical professionals when specific underlying pathology is expected.

The role of imaging in establishing a diagnosis is not clear. Based on the results of the literature review, the working group considers it highly plausible that this clinical diagnosis can be made without using additional imaging. In addition, from a recent international consensus meeting, it became clear that the majority of health care providers and patients (74% of the 60 participants) do not always consider imaging necessary for diagnosing Achilles tendinopathy.<sup>6</sup> However, the working group recognises that in the absence of systematically evaluated diagnostic criteria, imaging can be used to make diagnosis more or less likely and it can be useful when considering other differential diagnoses or specific underlying pathology. In cases with an unexpected clinical course or response to treatment, further diagnostic testing may be warranted. Another reason for additional imaging is to guide injection therapy or in the planning of a surgical procedure. Negative imaging results might also provide valuable information. It could trigger the healthcare provider to search for alternative diagnoses. When these cannot be identified, this phenomenon (localised tenderness with normal imaging) may be regarded as a subcategory of Achilles tendinopathy (early stage tendinopathy).<sup>5</sup>

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## Figures and Tables in supplementary file Module 2



**Figure 2.1** – PRISMA flowchart of the selection process for sub-question 2.1: What are the diagnostic criteria for Achilles tendinopathy?

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Embase.com	234	229
Medline ovid	258	101
Cochrane CENTRAL	31	13
<b>Total</b>	<b>523</b>	<b>343</b>

Database	Search terms
<b>Embase.com</b>	('achilles tendinitis'/exp OR ((tendinitis/de OR pathology/de) AND 'achilles tendon'/de) OR (((achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog*)):ab,ti) NOT ([Conference Abstract]/lim) AND [English]/lim NOT ([animals]/lim NOT [humans]/lim) AND ('sensitivity and specificity'/de OR 'observer variation'/exp OR 'interrater reliability'/de OR 'intrarater reliability'/de OR 'reproducibility'/exp OR 'discriminant analysis'/exp OR 'internal consistency'/de OR ((observer* NEAR/3 variation*) OR reproducib* OR reliab* OR unreliab* OR coefficient OR homogeneity OR homogeneous OR (internal* NEAR/3 consisten*) OR precision OR imprecision OR sensitivit* OR specificit* OR interrater* OR inter-rater* OR intrarater* OR intra-rater* OR intertester* OR inter-tester* OR intratester* OR intra-tester* OR interobserver* OR inter-observer* OR intraobserver* OR intra-observer* OR intertechnician* OR inter-technician* OR intratechnician* OR intra-technician* OR interexaminer* OR inter-examiner* OR intraexaminer* OR intra-examiner* OR interassay* OR inter-assay* OR intraassay* OR intra-assay* OR interindividual* OR inter-individual* OR intraindividual* OR intra-individual* OR interparticipant* OR inter-participant* OR intraparticipant* OR intra-participant* OR kappa OR kappa-s OR kappas OR repeatab* OR ((replicab* OR repeated) NEAR/3 (measure OR measures OR findings OR result OR results OR test OR tests)) OR generaliza* OR generalisa* OR concordance OR (intraclass NEAR/3 correlation*) OR discriminative OR error OR errors OR ((individual OR interval OR rate OR analysis OR values) NEAR/3 variabil*) OR (uncertainty NEAR/3 (measurement OR measuring)) OR 'standard error of measurement' OR sensitiv* OR interpretab* OR ((minimal OR minimally OR clinical OR clinically) NEAR/3 (important OR significant OR detectable) NEAR/3 (change OR difference)) OR (small* NEAR/3 (real OR detectable) NEAR/3 (change OR difference)) OR 'meaningful change' OR 'ceiling effect' OR 'floor effect' OR 'Item response model' OR IRT OR Rasch OR 'Differential item functioning' OR DIF OR 'computer adaptive testing' OR 'item bank' OR 'cross-cultural equivalence'):ab,ti)
<b>Medline ovid</b>	((('Tendinopathy/' OR Pathology/) AND "achilles tendon"/) OR "achilles tendon"/pa OR (((achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog*)):ab,ti) AND English.lg NOT (exp animals/ NOT humans/) AND ("Sensitivity and Specificity"/ OR Observer Variation/ OR Reproducibility of Results/ OR Discriminant Analysis/ OR ((observer* ADJ3 variation*) OR reproducib* OR reliab* OR unreliab* OR coefficient OR homogeneity OR homogeneous OR (internal* ADJ3 consisten*) OR precision OR imprecision OR sensitivit* OR specificit* OR interrater* OR inter-rater* OR intrarater* OR intra-rater* OR

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	<p>intertester* OR inter-tester* OR intratester* OR intra-tester* OR interobserver* OR inter-observer* OR intraobserver* OR intra-observer* OR intertechnician* OR inter-technician* OR intratechnician* OR intra-technician* OR interexaminer* OR inter-examiner* OR intraexaminer* OR intra-examiner* OR interassay* OR inter-assay* OR intraassay* OR intra-assay* OR interindividual* OR inter-individual* OR intraindividual* OR intra-individual* OR interparticipant* OR inter-participant* OR intraparticipant* OR intra-participant* OR kappa OR kappa-s OR kappas OR repeatab* OR ((replicab* OR repeated) ADJ3 (measure OR measures OR findings OR result OR results OR test OR tests)) OR generaliza* OR generalisa* OR concordance OR (intraclass ADJ3 correlation*) OR discriminative OR error OR errors OR ((individual OR interval OR rate OR analysis OR values) ADJ3 variabil*) OR (uncertainty ADJ3 (measurement OR measuring)) OR standard error of measurement OR sensitiv* OR interpretab* OR ((minimal OR minimally OR clinical OR clinically) ADJ3 (important OR significant OR detectable) ADJ3 (change OR difference)) OR (small* ADJ3 (real OR detectable) ADJ3 (change OR difference)) OR meaningful change OR ceiling effect OR floor effect OR Item response model OR IRT OR Rasch OR Differential item functioning OR DIF OR computer adaptive testing OR item bank OR cross-cultural equivalence).ab,ti.)</p>
<b>Cochrane CENTRAL</b>	<p>(((((achilles OR calcaneal) AND (tendinitis* OR tendinopath* OR tendinosis* OR tendonitis* OR tendon-patholog*)))ab,ti) AND (((observer* NEAR/3 variation*) OR reproducib* OR reliab* OR unreliab* OR coefficient OR homogeneity OR homogeneous OR (internal* NEAR/3 consisten*) OR precision OR imprecision OR sensitivit* OR specificit* OR interrater* OR inter-rater* OR intrarater* OR intra-rater* OR intertester* OR inter-tester* OR intratester* OR intra-tester* OR interobserver* OR inter-observer* OR intraobserver* OR intra-observer* OR intertechnician* OR inter-technician* OR intratechnician* OR intra-technician* OR interexaminer* OR inter-examiner* OR intraexaminer* OR intra-examiner* OR interassay* OR inter-assay* OR intraassay* OR intra-assay* OR interindividual* OR inter-individual* OR intraindividual* OR intra-individual* OR interparticipant* OR inter-participant* OR intraparticipant* OR intra-participant* OR kappa OR kappa-s OR kappas OR repeatab* OR ((replicab* OR repeated) NEAR/3 (measure OR measures OR findings OR result OR results OR test OR tests)) OR generaliza* OR generalisa* OR concordance OR (intraclass NEAR/3 correlation*) OR discriminative OR error OR errors OR ((individual OR interval OR rate OR analysis OR values) NEAR/3 variabil*) OR (uncertainty NEAR/3 (measurement OR measuring)) OR 'standard error of measurement' OR sensitiv* OR interpretab* OR ((minimal OR minimally OR clinical OR clinically) NEAR/3 (important OR significant OR detectable) NEAR/3 (change OR difference)) OR (small* NEAR/3 (real OR detectable) NEAR/3 (change OR difference)) OR 'meaningful change' OR 'ceiling effect' OR 'floor effect' OR 'Item response model' OR IRT OR Rasch OR 'Differential item functioning' OR DIF OR 'computer adaptive testing' OR 'item bank' OR 'cross-cultural equivalence'):ab,ti)</p>

**Table 2.1** – Search strategy for diagnostic criteria (sub-question 1)



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Clinical criteria used	Number of studies
• Pain on palpation	17/26
• Symptoms localised to 2-7 cm proximal from the Achilles tendon insertion	13/26
• Thickening of the tendon	11/26
• Pain during or after exercise	8/26
• History of pain	7/26
• Morning stiffness/starting stiffness	5/26
• Functional limitations	4/26
• Reduced symptoms if tendon under tension	1/26
• VISA-A score (no cut off value reported)	1/26
• VAS score (no cut off value reported)	1/26

**Table 2.2** – Criteria used for diagnosing midportion Achilles tendinopathy in 26 trials.

Clinical criteria used	Number of studies
• Pain on palpation of the Achilles tendon insertion	2/3
• Reduced tendon loading capacity	2/3
• No criteria reported	1/3

**Table 2.3** – Criteria for diagnosing insertional Achilles tendinopathy used in 3 trials.

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Study	Clinical criteria	Imaging
<b>Midportion Achilles tendinopathy</b>		
Balius, 2016 <sup>10</sup>	<ul style="list-style-type: none"> <li>• Painful thickening of the Achilles tendon located 2 to 6 cm above the tendon insertion</li> <li>• Symptoms present for at least 3 months</li> </ul>	• Ultrasonography
Bell, 2013 <sup>11</sup>	<ul style="list-style-type: none"> <li>• Chronic localised pain and stiffness</li> <li>• Symptoms present for at least 3 months</li> </ul>	• Ultrasonography
Beyer, 2015 <sup>12</sup>	<ul style="list-style-type: none"> <li>• Diagnosis based on VISA-A score, VAS-score, physical examination, and pain. Specific criteria were not reported</li> <li>• Symptoms present for at least 3 months</li> </ul>	• Ultrasonography
Boesen, 2017 <sup>13</sup>	<ul style="list-style-type: none"> <li>• Thickness and pain on clinical examination located 2-7 cm proximal to the insertion on the calcaneus</li> <li>• Symptoms present for at least 3 months</li> </ul>	• Ultrasonography
de Jonge, 2010 <sup>14</sup>	<ul style="list-style-type: none"> <li>• Tendon painful on palpation and painful during or after sport</li> <li>• Tendon thickening 2-7 cm proximal to the distal insertion</li> <li>• Symptoms present for at least 2 months</li> </ul>	• None
de Jonge, 2011 <sup>15</sup>	<ul style="list-style-type: none"> <li>• Tendon painful on palpation and painful during or after sport</li> <li>• Tendon thickening 2-7 cm proximal to the distal insertion</li> <li>• Symptoms present for at least 2 months</li> </ul>	• None
Heinemeier, 2017 <sup>16</sup>	<ul style="list-style-type: none"> <li>• Pain during Achilles tendon loading</li> <li>• Clinical signs of midportion Achilles tendinopathy (not further specified)</li> <li>• Symptoms present for at least 3 months</li> </ul>	• Ultrasonography
Herrington, 2007 <sup>17</sup>	<ul style="list-style-type: none"> <li>• Complaints of local Achilles pain, stiffness or functional impairment on activity</li> <li>• Symptoms present for at least 3 months</li> </ul>	• None
Hutchison, 2013 <sup>18</sup>	<ul style="list-style-type: none"> <li>• Pain and tenderness in the tendo Achilles between 2 cm and 6 cm above its insertion into the calcaneum</li> <li>• Symptoms present for at least 3 months</li> </ul>	• Ultrasonography
Krogh, 2016 <sup>19</sup>	<ul style="list-style-type: none"> <li>• Painful and thickened tendon in relation to activity and on palpation (2 to 7 cm proximal to the insertion on the calcaneus)</li> <li>• Symptoms present for at least 6 months</li> </ul>	• Ultrasonography
Lynen, 2017 <sup>20</sup>	<ul style="list-style-type: none"> <li>• Painful midportion Achilles tendon (area not further specified)</li> <li>• Symptoms present for at least 6 weeks</li> </ul>	• None
Morrison, 2017 <sup>21</sup>	<ul style="list-style-type: none"> <li>• Criteria not reported</li> <li>• Symptoms present for at least 6 months</li> </ul>	• MRI
Munteanu, 2015 <sup>22</sup>	<ul style="list-style-type: none"> <li>• Insidious onset of pain in the Achilles tendon region aggravated by weightbearing activities and/or was worse in the morning and/or during the initial stages of weightbearing activities; and pain located 2-6 cms proximal to the Achilles tendon insertion</li> <li>• Symptoms present for at least 3 months</li> </ul>	• Ultrasonography
Mafi, 2001 <sup>23</sup>	<ul style="list-style-type: none"> <li>• Painful area 2-6 cm from the calcaneal insertion</li> </ul>	• Ultrasonography
Pearson,	<ul style="list-style-type: none"> <li>• Activity-related pain of gradual or semiacute onset,</li> </ul>	• None

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2012 <sup>24</sup>	<p>postinactivity stiffness, and tenderness, thickening, and nodularity localised to the midtendon</p> <ul style="list-style-type: none"> <li>• Symptoms present for at least 3 months</li> </ul>	
Rompe, 2007 <sup>25</sup>	<ul style="list-style-type: none"> <li>• Pain over the main body of the Achilles tendon 2 to 6 cm proximal to its insertion, thickening, and impaired function</li> <li>• Symptoms present for at least 6 months</li> </ul>	• Ultrasonography
Rompe, 2009 <sup>26</sup>	<ul style="list-style-type: none"> <li>• Pain over the main body of the Achilles tendon 2 to 6 cm proximal to its insertion, thickening, and impaired function</li> <li>• Symptoms present for at least 6 months</li> </ul>	• Ultrasonography
Roos, 2004 <sup>27</sup>	<ul style="list-style-type: none"> <li>• Symptoms located 2-6 cm proximally to the insertion</li> <li>• Symptoms present for at least 4 weeks</li> </ul>	• None
Silbernagel, 2001 <sup>28</sup>	<ul style="list-style-type: none"> <li>• Chronic pain from the Achilles tendon</li> <li>• Symptoms present for at least 3 months</li> </ul>	• None
Silbernagel, 2007 <sup>29</sup>	<ul style="list-style-type: none"> <li>• Achilles tendon pain, thickening, and impaired performance</li> <li>• Symptoms present for at least 2 months</li> </ul>	• None
Stevens, 2014 <sup>30</sup>	<ul style="list-style-type: none"> <li>• Midportion Achilles tenderness (2-7 cm proximal to insertion) on palpation during or after activity</li> <li>• Symptoms present for at least 3 months</li> </ul>	• None
Tumilty, 2012 <sup>31</sup>	<ul style="list-style-type: none"> <li>• Tender area of intratendinous thickening that moves with the tendon and significantly decreases or disappears when the tendon is put under tension</li> <li>• Symptoms present for at least 3 months</li> </ul>	• None
Tumilty, 2016 <sup>32</sup>	<ul style="list-style-type: none"> <li>• Tender area of intratendinous thickening that moves with the tendon and significantly decreases or disappears when the tendon is put under tension</li> <li>• Symptoms present for at least 3 months</li> </ul>	• None
Uselli, 2017 <sup>33</sup>	<ul style="list-style-type: none"> <li>• Criteria not reported</li> <li>• Symptoms present for at least 3 months</li> </ul>	• None
Yelland, 2011 <sup>34</sup>	<ul style="list-style-type: none"> <li>- Pain 2-7 cm proximal to the calcaneal attachment</li> <li>- Symptoms present for at least 6 weeks</li> </ul>	- None
Zhang, 2013 <sup>35</sup>	<ul style="list-style-type: none"> <li>- Pain during and after physical activity, tenderness on palpation and morning stiffness, and thickening.</li> <li>- Painful and thickened tendon in relation to activity and on palpation 2-7 cm proximal to the insertion on the calcaneus</li> <li>- Symptoms present for at least 2 months</li> </ul>	- None
<b>Insertional Achilles tendinopathy</b>		
Hunt, 2015 <sup>36</sup>	<ul style="list-style-type: none"> <li>• Criteria not reported</li> <li>• Symptoms present for at least 6 months</li> </ul>	• Not reported
Njawaya, 2017 <sup>37</sup>	<ul style="list-style-type: none"> <li>• Pain and impaired function</li> </ul>	• Ultrasonography
Rompe, 2008 <sup>38</sup>	<ul style="list-style-type: none"> <li>• Localised pain over the distal part of the Achilles tendon at its insertion onto the calcaneus, with local tenderness and a reduced level of activity</li> <li>• Symptoms present for at least 6 months</li> </ul>	• Ultrasonography
<b>Achilles tendinopathy (not further specified)</b>		

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Auclair, 1989 <sup>39</sup>	- Criteria not reported • Symptoms present <1 month	• Not reported
Ebbesen, 2018 <sup>40</sup>	• Pain on the Achilles tendon • Symptoms present for at least 3 months	• Ultrasonography

**Table 2.4** – Clinical and criteria and type of imaging modality used in the included randomised trials in the treatment module.

<b>Musculotendinous entities</b>
• Plantaris tendinopathy or rupture
• Plantar fasciopathy or fascia rupture
• Tendinopathy of the flexor tendons of the toes or ankle
• Rupture of the crural fascia
• Accessory soleus muscle
• Exercise-related compartment syndrome of the deep flexor compartment
• Soft tissue tumour
<b>Bony entities</b>
• Stress fracture of the calcaneus
• Bone tumour of the calcaneus
• Infectious pathology of the calcaneus (e.g. Brodies abscess)
<b>Joint entities</b>
• Posterior ankle impingement
• Chondral pathology of the subtalar joint
<b>Neurological entities</b>
• Neuropathy of the sural nerve
• Tarsal tunnel syndrome

**Table 2.5** – Differential diagnostic considerations for posterior ankle pain.

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Midportion	Insertional
<b>Mechanical cause</b>	
<ul style="list-style-type: none"> <li>• Achilles tendon rupture (partial or complete)</li> </ul>	<ul style="list-style-type: none"> <li>• Achilles tendon rupture (partial or complete)</li> </ul>
<ul style="list-style-type: none"> <li>• Calcifying Achilles tendinopathy</li> </ul>	<ul style="list-style-type: none"> <li>• Calcifying Achilles tendinopathy</li> </ul>
<ul style="list-style-type: none"> <li>• Plantaris tendon mediated Achilles tendinopathy (medially localised Achilles tendinopathy due to invagination of the plantaris tendon)</li> </ul>	<ul style="list-style-type: none"> <li>• Retrocalcaneal bursitis with or without Haglund's morphology</li> </ul>
<ul style="list-style-type: none"> <li>• Paratendinopathy of the Achilles tendon</li> </ul>	<ul style="list-style-type: none"> <li>• Subcutaneous Achilles bursitis</li> </ul>
	<ul style="list-style-type: none"> <li>• Paratendinopathy of the Achilles tendon</li> </ul>
	<ul style="list-style-type: none"> <li>• Morbus Sever (children and adolescents)</li> </ul>
<b>Inflammatory cause</b>	
	Enthesitis related to auto-inflammatory arthropathies (axial spondyloarthritis, reactive arthritis and psoriatic arthritis)
<b>Metabolic-induced cause</b>	
Tendinopathy related to metabolic disorders (Diabetes Mellitus, hypercholesterolemia, gout)	
Tendon xanthomas as part of Familial Hypercholesterolemia)	
<b>Medication-induced cause</b>	
Medication induced tendinopathy (fluoroquinolone antibiotics)	

**Table 2.6** – Associated pathologies for midportion and insertional Achilles tendinopathy.

## Consensus statement

Achilles tendinopathy in the context of rheumatological disease

Insertional Achilles tendinopathy can occur in relation to specific rheumatological conditions. In spondylarthritis, a group of rheumatological inflammatory disorders in which inflammation can occur in both the spine and in the peripheral joints, enthesitis is a frequent manifestation and can present clinically as insertional Achilles tendinopathy.

Spondylarthritis (SpA) are a group of rheumatological diseases in which enthesitis, arthritis and dactylitis are associated with psoriasis, sacroiliitis or inflammatory bowel disease (IBD). Specific SpA subtypes are axial spondylarthritis in which chronic low back pain due to sacroiliitis is the hallmark and in which Achilles tendon enthesitis can be a symptom. In psoriatic arthritis and in arthritis related to inflammatory bowel diseases (IBD), Achilles tendon enthesitis can also occur.

The prevalence of SpA in Europe is estimated at 0.54%.<sup>41</sup> Estimates of the life time prevalence of Achilles tendon enthesitis was 47% in a cohort of 275 SpA patients.<sup>42 37 11 37 92 94 110 114 114 11442</sup>

Recognition of Achilles tendon enthesitis in the context of SpA is important because of its possible destructive nature and the debilitating effects that the disease can have. In addition, proven effective anti-inflammatory treatment options are available. Early drug treatment can have a beneficial long-term effect on outcomes. It is not inconceivable that an Achilles tendon enthesitis is the first and most glaring symptom in a patient with SpA who consults a healthcare provider with Achilles tendon pain.

Differentiating between an inflammatory origin of an insertional Achilles tendinopathy and other causes is often very difficult in clinical practice. Symptoms of Achilles tendon enthesitis related to SpA are often identical to the symptoms due to other causes of insertional Achilles tendinopathy. Inflammatory characteristics of symptoms are morning stiffness and nocturnal pain which can be less pronounced in mechanical (overuse) tendinopathy. In addition to pain on palpation and tendon thickening, physical examination can also reveal a localised high skin temperature as an inflammatory symptom. Inflammatory characteristics on MRI or ultrasound do not appear to be able to distinguish between enthesitis in the context of SpA and insertional tendinopathy due to other (mechanical) causes. Possible structural abnormalities are considered a late manifestation of the condition and are therefore less suitable for a shorter symptom duration.<sup>43</sup>

The risk of Achilles enthesitis in the context of SpA increases when, in addition to an insertional Achilles tendinopathy, there are also (possibly) other characteristics of SpA. Pattern recognition of characteristics of SpA is the foundation for the strategies for rheumatological evaluation in the context of the early recognition of SpA in patients with combinations of arthritis, enthesitis or dactylitis and psoriasis or chronic low back pain.<sup>44</sup>

*Conclusion*

An insertional Achilles tendinopathy can have a rheumatological origin. Achilles tendon enthesitis can occur in the context of spondylarthritis; a group of rheumatological diseases with axial spondylarthritis and psoriatic arthritis as subtypes. For these specific diagnoses, anti-inflammatory drug therapy may be indicated to improve chronicity of symptoms.

*Considerations*

These recommendations are in accordance with (inter)national recommendations.

*Recommendations*

1. Refer patients with insertional Achilles tendinopathy and an established diagnosis of spondylarthritis for rheumatological evaluation
2. Consider referring the following patients for rheumatological evaluation: patients with insertional Achilles tendinopathy without a known diagnosis of spondylarthritis but who have chronic low back that started before the age of 45 or associated psoriasis.

Achilles tendinopathy as a result of Familial Hypercholesterolemia

Achilles tendinopathy can have a metabolic cause. Especially in familial hypercholesterolemia (FH), midportion Achilles tendinopathy occur.<sup>45</sup>

## Consensus statement

FH is a monogenetic, autosomal dominant inherited disorder and is characterised by high LDL cholesterol levels or markedly raised total cholesterol levels.<sup>46</sup> Untreated, this mutation often leads to death at a relatively young age due to cardiovascular disease. Other clinical manifestations of FH include cholesterol depositions in the cornea (arcus lipoides) and tendons (xanthomas). These tendon xanthomas can lead to midportion Achilles tendinopathy. Distinguishing features are the multiple noduli that can be palpable in the tendon and a lobular structure of the Achilles tendon on MRI with dotted hyperintense signal intensities on the T1-weighted images.<sup>45</sup>

It is possible that Achilles tendon pain is the initial manifestation in a patient with FH. Recognition of a xanthoma of the Achilles tendon in the context of FH is important due to the fact that FH has a high mortality rate when left untreated. There is strong evidence that early drug treatment leads to a more favourable long-term outcome.<sup>47</sup> Tendon related symptoms also disappear over time after treatment for FH.<sup>45</sup>

Differentiation between an overuse (mechanical) midportion Achilles tendinopathy and a tendon xanthoma in the context of FH can be difficult. A number of characteristics can increase the chance of FH as the underlying cause of the Achilles tendon problem:<sup>47</sup>

- an untreated LDL cholesterol value higher than 5.0 mmol/l or an untreated total cholesterol value higher than 8.0 mmol/l;
- a first-degree relative member with cardiovascular disease before the age of 60;
- a first-degree relative member with an untreated total cholesterol level higher than 7.0 mmol/l, approximately equivalent to an LDL cholesterol level higher than 5.0 mmol/l;
- an expression of cardiovascular disease in the patient themselves before the age of 60;
- the presence of an arcus lipoides before the age of 45.

#### Conclusion

A midportion Achilles tendinopathy may be an expression of an Achilles tendon xanthoma related to FH. FH is classified by high LDL or total cholesterol levels, cardiovascular diseases and/or high cholesterol levels in first-degree relatives before the age of 60, cardiovascular disease before the age of 60 and arcus lipoides before the age of 45. Treatment of FH with statins has an important effect on the risk of cardiovascular events and mortality.

#### Recommendations

1. Consider referring for evaluation by internal medicine specialist:  
Patients with midportion Achilles tendinopathy and an established FH
2. Consider referring for evaluation:  
Patients with midportion Achilles tendinopathy without an established diagnosis of FH, who have a high LDL or total cholesterol levels, cardiovascular diseases and/or high cholesterol levels in first-degree relatives before the age of 60, cardiovascular disease in the patient themselves before the age of 60 or the presence of arcus lipoides before the age of 45

**Table 2.7** – Achilles tendinopathy in spondylarthritis and Familial Hypercholesterolemia.

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